



Complete Summary

GUIDELINE TITLE

(1) Medical therapy for pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. (2) 2007 addendum.

BIBLIOGRAPHIC SOURCE(S)

Badesch DB, Abman SH, Ahearn GS, Barst RJ, McCrory DC, Simonneau G, McLaughlin VV. Medical therapy for pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Chest 2004 Jul; 126(1 Suppl): 35S-62S. [191 references] [PubMed](#)

Badesch DB, Abman SH, Simonneau G, Rubin LJ, McLaughlin VV. Medical therapy for pulmonary arterial hypertension: updated ACCP evidence-based clinical practice guidelines. Chest 2007 Jun; 131(6):1917-28. [34 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [August 16, 2007, Coumadin \(Warfarin\)](#): Updates to the labeling for Coumadin to include pharmacogenomics information to explain that people's genetic makeup may influence how they respond to the drug.
- [October 6, 2006, Coumadin \(warfarin sodium\)](#): Revisions to the labeling for Coumadin to include a new patient Medication Guide as well as a reorganization and highlighting of the current safety information to better inform providers and patients.
- [March 2, 2006, Tracleer \(bosentan\)](#): Changes to the prescribing information based on cases of hepatotoxicity reported.
- [July 8, 2005, Cialis \(tadalafil\), Levitra \(vardenafil hydro chloride\) and Viagra \(sildenafil citrate\)](#): Updated labeling for Cialis, Levitra and Viagra to reflect a small number of post-marketing reports of sudden vision loss.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

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BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
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DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Pulmonary arterial hypertension

GUIDELINE CATEGORY

Treatment

CLINICAL SPECIALTY

Cardiology
Internal Medicine
Pediatrics
Pulmonary Medicine
Rheumatology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To provide appropriate evidence-based treatment recommendations for physicians involved in the care of patients with pulmonary arterial hypertension
- To provide an update to the previously published (2004) guidelines on medical therapy for pulmonary arterial hypertension

TARGET POPULATION

Adults and children with pulmonary arterial hypertension

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment

1. Acute vasoreactivity testing using short-acting agents, such as intravenous epoprostenol or adenosine or inhaled nitric oxide
2. Pharmacotherapy
 - Oral calcium channel blockers (e.g., nifedipine, diltiazem, amlodipine)
 - Anticoagulation with warfarin
 - Supplemental oxygen as needed
 - Enrollment in clinical trials as appropriate
 - Endothelin-receptor antagonists (bosentan)
 - Intravenous epoprostenol
 - Intravenous treprostinil
 - Subcutaneous treprostinil
 - Inhaled iloprost
 - Sildenafil
3. Special considerations for children, pregnant women, patients with portopulmonary hypertension, and patients with human immunodeficiency virus (HIV) infection (see "Major Recommendations" field).

MAJOR OUTCOMES CONSIDERED

- Exercise capacity (e.g., median distance walked in 6 minutes)
- Changes in cardiopulmonary hemodynamics
- Pulmonary function
- Survival
- Borg dyspnea scores and dyspnea-fatigue ratings
- Severity of Raynaud's phenomenon and digital ulcers
- Quality of life
- Changes in World Health Organization functional class
- Side effects of therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

2004 Guideline

Note from National Guideline Clearinghouse (NGC): The Center for Clinical Health Policy Research at Duke University identified and evaluated evidence on this topic, working with the guideline development panel to formulate key questions suitable for systematic literature synthesis.

Search Strategy

Computerized searches of the MEDLINE bibliographic database from 1992 to October 2002 were conducted. The developer searched using the term hypertension, pulmonary. The search was limited to articles concerning human

subjects that were published in the English language and accompanied by an abstract. In addition, the developer searched the reference lists of included studies, practice guidelines, systematic reviews, and meta-analyses, and consulted with clinical experts to identify relevant studies missed by the search strategy or published before 1992.

Study Selection

For the topic on treatment, the guideline developer selected studies of oxygen, diuretics, inotropic agents (digoxin), anticoagulants, calcium antagonists, angiotensin-converting enzyme inhibitors, prostanoids (e.g., epoprostenol, treprostinil, inhaled iloprost), L-arginine, endothelin-receptor antagonists (e.g., bosentan, sitaxsentan, ambrisentan), phosphodiesterase-5 inhibitors (sildenafil), nitric oxide (NO), and thromboxane inhibitors (e.g., terbogrel). The guideline developer considered studies conducted among patients with known or suspected idiopathic pulmonary arterial hypertension (IPAH) or pulmonary arterial hypertension (PAH) occurring in association with underlying collagen vascular disease, congenital heart disease, or chronic thromboembolic disease. The guideline developers excluded studies of pulmonary hypertension (PH) associated with chronic obstructive pulmonary disease (COPD) or other parenchymal lung disease, high-altitude PH, or cardiac disease (e.g., left-heart failure, valvular heart disease) except congenital heart disease. The summary evidence tables can be viewed on-line at http://www.chestjournal.org/content/vol126/1_suppl/.

2007 Addendum

The authors performed computerized searches of the literature for studies on the medical treatment of PAH that were published prior to September 1, 2006. Only English-language articles were included. They selected studies of therapeutic agents in the following classes: prostanoids, endothelin receptor antagonists, and phosphodiesterase inhibitors. As in the previous guidelines, they considered studies conducted among patients with known or suspected IPAH or PAH occurring in association with underlying collagen vascular disease, and congenital heart disease. Also in a manner consistent with the previous statement, they excluded studies of PH associated with COPD or other parenchymal lung disease, high-altitude PH, or cardiac disease (e.g., left-heart failure, valvular heart disease) except congenital heart disease.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of the Evidence

Good = evidence based on good randomized controlled trials or meta-analyses

Fair = evidence based on other controlled trials or randomized controlled trials with minor flaws

Low = evidence based on nonrandomized, case-control, or other observational studies

Expert opinion = evidence based on the consensus of the carefully selected panel of experts in the topic field. There are no studies that meet the criteria for inclusion in the literature review.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

2004 Guideline

An international panel of 19 experts representing five medical specialties was assembled. Representatives from other medical and patient advocacy associations were also invited to join the panel (including the American College of Cardiology, American College of Rheumatology, and the Pulmonary Hypertension Association). These experts convened on several occasions, including the culminating panel conference in September 2003, in which they deliberated over the composition of the final recommendations and grading of the current state of the evidence, benefits to the patient, and the strength of the recommendations.

Guideline development was led by an executive committee including the chair, the leader of the methodology support group, and the American College of Chest Physicians (ACCP) project manager, which supervised the guideline development process, methodologic issues, panel composition, structure of the final document, and activities of the writing committees. Each writing committee, led by a group leader who served as primary author and editor of that chapter, conferred with the methodology team on inclusion/exclusion criteria, relevant research questions, and important literature that was not readily identified. These individuals continue with their responsibilities to assist in the development of the implementation tools.

When the evidence was insufficient for evidence-based recommendations, the panel used informal group consensus techniques to develop recommendations based on the expert opinion of the panel. With every member of the panel attending the final conference, the expert-based opinions are truly representative of geographically diverse and multispecialty inclusive practice patterns of the complete panel.

2007 Addendum

A consensus panel convened by the ACCP developed guidelines for the diagnosis and treatment of pulmonary arterial hypertension (PAH) that were published in 2004. Subsequently, several important clinical trials have been published and new treatments have received regulatory approval. In addition, add-on and combination therapy are being explored, which promise to open new therapeutic avenues.

Therefore, the Health and Science Policy Committee of the ACCP authorized an update of the medical treatment guidelines. The same individual was again selected to chair the panel. A small subset of authors from the original guideline were requested to participate in the update. In October 2005, the group met in Montreal to plan the revision and to cultivate consensus on the approach to the new treatment algorithm.

This addendum provides an update to the previously published guidelines based on the current body of literature. The original guidelines have been summarized, a discussion of new studies has been added, and the treatment algorithm has been revised to take into account recent developments in therapy. The recommendations in this guideline, like those in the 2004 edition, are based on the same grading system, in which the strength of the recommendation results from the interaction of two components: the quality of the evidence, and the net benefit of the therapy to the patient (see "Rating Scheme for the Strength of the Recommendations").

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendations

A = strong recommendation
B = moderate recommendation
C = weak recommendation
D = negative recommendation
I = no recommendation possible (inconclusive)
E/A = strong recommendation based on expert opinion only
E/B = moderate recommendation based on expert opinion only
E/C = weak recommendation based on expert opinion only
E/D = negative recommendation based on expert opinion only

Net Benefit

Substantial
Intermediate

Small/weak
None
Conflicting
Negative

Relationship of Strength of the Recommendations Scale to Quality of Evidence and Net Benefits

	Net Benefit					
Quality of Evidence	Substantial	Intermediate	Small/Weak	None	Conflicting	Negative
Good	A	A	B	D	I	D
Fair	A	B	C	D	I	D
Low	B	C	C	I	I	D
Expert opinion	E/A	E/B	E/C	I	I	E/D

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

2004 Guideline

The writing groups and the executive committee of the panel extensively reviewed each chapter during the writing process. The final conference provided an opportunity for the entire panel to review the latest drafts. Following final revisions and one final review by the executive committee, each chapter of the guidelines was reviewed and approved by the American College of Chest Physicians (ACCP) Health and Science Policy Committee, the ACCP Pulmonary Vascular NetWork, and then by the ACCP Board of Regents. The guidelines have not been field tested.

2007 Addendum

This guideline was reviewed and approved by the Pulmonary Vascular NetWork, Health and Science Policy Committee, and ultimately by the Board of Regents of the ACCP.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from National Guideline Clearinghouse (NGC) and American College of Chest Physicians (ACCP): In June 2007, the ACCP released an update to their guidelines on medical therapy for pulmonary arterial hypertension, taking into consideration studies published prior to September 1, 2006. Recommendations that have been changed since the original 2004 guideline are displayed below in italics.

Rating schemes for level of evidence, strength of recommendation, and net benefit follow the major recommendations.

1. Patients with idiopathic pulmonary arterial hypertension (IPAH) should undergo acute vasoreactivity testing using a short-acting agent such as intravenous (IV) epoprostenol, adenosine, or inhaled nitric oxide (NO). Level of evidence: fair; benefit: substantial; grade of recommendation: A.
2. Patients with pulmonary arterial hypertension (PAH) associated with underlying processes, such as scleroderma or congenital heart disease, should undergo acute vasoreactivity testing. Level of evidence: expert opinion; benefit: small/weak; grade of recommendation: E/C.
3. Patients with PAH should undergo vasoreactivity testing by a physician experienced in the management of pulmonary vascular disease. Level of evidence: expert opinion; benefit: substantial; grade of recommendation: E/A.
4. Patients with IPAH, in the absence of right-heart failure, demonstrating a favorable acute response to vasodilator (defined as a fall in mean pulmonary arterial pressure [mPAP] of at least 10 mm Hg to ≤ 40 mm Hg, with an increased or unchanged cardiac output [CO]), should be considered candidates for a trial of therapy with an oral calcium-channel antagonist. Level of evidence: low; benefit: substantial; grade of recommendation: B.
5. Patients with PAH associated with underlying processes such as scleroderma or congenital heart disease, in the absence of right-heart failure, demonstrating a favorable acute response to vasodilator (defined as a fall in mean pulmonary arterial pressure [mPAP] of at least 10 mm Hg to ≤ 40 mm Hg, with an increased or unchanged CO), should be considered candidates for a trial of therapy with an oral calcium-channel antagonist. Level of evidence: expert opinion; benefit: intermediate; grade of recommendation: E/B.
6. In patients with PAH, calcium-channel blockers (CCBs) should not be used empirically to treat pulmonary hypertension (PH) in the absence of demonstrated acute vasoreactivity. Level of evidence: expert opinion; benefit: substantial; grade of recommendation: E/A.
7. Patients with IPAH should receive anticoagulation with warfarin. Level of evidence: fair; benefit: intermediate; grade of recommendation: B.
8. In patients with PAH occurring in association with other underlying processes, such as scleroderma or congenital heart disease, anticoagulation should be considered. Level of evidence: expert opinion; benefit: small/weak; recommendation: E/C.
9. In patients with PAH, supplemental oxygen should be used as necessary to maintain oxygen saturations at $>90\%$ at all times. Level of evidence: expert opinion; benefit: substantial; recommendation: E/A.
10. PAH patients in functional class II who are not candidates for, or who have failed, CCB therapy, may benefit from treatment with:

- a. Sildenafil. Level of evidence: good; benefit: substantial; grade of recommendation: A
 - b. Subcutaneous treprostinil. Level of evidence: low; benefit: small/weak; grade of recommendation: C. Although treprostinil is U.S. Food and Drug Administration (FDA) approved for use in patients in functional class II, it would seldom be recommended in such patients due to the complexity of administration, side effects, and cost.
 - c. IV treprostinil. Level of evidence: low; benefit: small/weak; grade of recommendation: C. Although treprostinil is U.S. Food and Drug Administration (FDA) approved for use in patients in functional class II, it would seldom be recommended in such patients due to the complexity of administration, side effects, and cost.
 - d. Data pertaining to the treatment of functional class II patients remain limited, and enrollment in clinical trials is encouraged.
11. PAH patients in functional class III who are not candidates for, or who have failed, CCB therapy are candidates for long-term therapy with:
- a. Endothelin-receptor antagonists (bosentan), or sildenafil, in no order of preference. Level of evidence: good; benefit: substantial; grade of recommendation: A.
 - b. IV epoprostenol. Level of evidence: good; benefit: substantial; grade of recommendation: A.
 - c. Inhaled iloprost. Level of evidence: good; benefit: intermediate; grade of recommendation: A.
 - d. Subcutaneous treprostinil. Level of evidence: fair; benefit: intermediate; grade of recommendation: B.
 - e. IV treprostinil. Level of evidence: low; benefit: intermediate; grade of recommendation: C.
12. PAH patients in functional class IV who are not candidates for, or who have failed, CCB therapy are candidates for long-term therapy with IV epoprostenol (treatment of choice). Level of evidence: good; benefit: substantial; grade of recommendation: A.
13. Other treatments available for the treatment of functional class IV PAH include, in no hierarchical order:
- a. Endothelin-receptor antagonists (bosentan). Level of evidence: fair; benefit: intermediate; grade of recommendation: B.
 - b. Inhaled iloprost. Level of evidence: fair; benefit: intermediate; grade of recommendation: B.
 - c. Subcutaneous treprostinil. Level of evidence: fair; benefit: intermediate; grade of recommendation: B.
 - d. Sildenafil. Level of evidence: low; benefit: Intermediate; grade of recommendation: C.
 - e. IV treprostinil. Level of evidence: low; benefit: intermediate; grade of recommendation: C.
14. 2004 recommendation has been deleted.
15. 2004 recommendation has been deleted.
16. Children with PAH:
- a. With right-heart failure or with a hypercoagulable state should receive anticoagulation with warfarin. Level of evidence: expert opinion; net benefit: intermediate; strength of recommendation: E/B.

- b. Without right-heart failure or a hypercoagulable state may receive anticoagulation with warfarin; for children <5 years of age, lower target international normalized ratios (INRs) are recommended. Level of evidence: expert opinion; net benefit: small/weak; strength of recommendation: E/C.

17. In patients with PAH, pregnancy should be avoided, or termination recommended. Level of evidence: good; benefit: substantial; grade of recommendation: A.

Definitions:

Quality of the Evidence

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Strength of Recommendations

A = strong recommendation

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I = no recommendation possible (inconclusive)

E/A = strong recommendation based on expert opinion only

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Net Benefit

Substantial

Intermediate

Small/weak

None

Conflicting

Negative

Relationship of Strength of the Recommendations Scale to Quality of Evidence and Net Benefits

	Net Benefit
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Quality of Evidence	Substantial	Intermediate	Small/Weak	None	Conflicting	Negative
Good	A	A	B	D	I	D
Fair	A	B	C	D	I	D
Low	B	C	C	I	I	D
Expert opinion	E/A	E/B	E/C	I	I	E/D

CLINICAL ALGORITHM(S)

An updated clinical algorithm is provided in the addendum to the original guideline document for treatment of pulmonary arterial hypertension.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate treatment of pulmonary arterial hypertension
- Improved exercise capacity, quality of life, and survival in patients with pulmonary arterial hypertension

POTENTIAL HARMS

- Risks of adverse effects, including death, during vasoreactivity testing
- Risk of gastrointestinal bleeding with anticoagulants
- Rapid and excessive diuresis may lead to systemic hypotension, renal insufficiency, and syncope.
- Epoprostenol therapy is complicated by the need for continuous intravenous infusion. Due to the long duration of therapy and the ongoing risk of catheter-associated infection, tunneled central venous catheters are generally preferred. Common side effects of epoprostenol therapy include headache, flushing, jaw pain with initial mastication, diarrhea, nausea, a blotchy erythematous rash, and musculoskeletal aches and pain (predominantly involving the legs and feet). These tend to be dose dependent and often respond to a cautious reduction in dose. Severe side effects can occur with overdosage of the drug. Acutely, overdosage can lead to systemic hypotension. Long-term overdosage can lead to the development of a hyperdynamic state and high-output cardiac failure. Abrupt or inadvertent interruption of the epoprostenol infusion should be avoided, as this may, in some patients, lead to a rebound worsening of their pulmonary hypertension with symptomatic deterioration and perhaps even death.
- The nemesis of subcutaneous treprostinil has been pain and erythema at the infusion site.
- Overall, inhaled iloprost is well tolerated; in one placebo-controlled study, cough, flushing, and headache occurred more frequently in the iloprost group

than in the placebo group. These adverse events were mild and mostly transient. Syncope occurred with similar frequency in the two groups, but was more frequently considered to be serious in the iloprost group, although this adverse effect was not associated with clinical deterioration.

- There are several notable potential toxicities associated with the use of bosentan. Due to the risk of potential hepatic toxicity, the U.S. Food and Drug Administration requires that liver function tests be performed at least monthly in patients receiving this drug. Bosentan use may also be associated with the development of anemia, which seems typically to be mild. The hemoglobin/hematocrit should be checked regularly. Due to the potential teratogenic effects of bosentan, careful attention must be paid to the use of adequate contraception in women of childbearing age. It is important to note that bosentan may decrease the efficacy of hormonal contraceptive techniques, and for this reason they should not be used alone. Rather, it is suggested that some other form of contraception be included, such as the use of double-barrier techniques (condom and diaphragm) with a spermicide. Regular pregnancy testing is recommended in women of childbearing age. There is concern that the endothelin antagonists as a class may be capable of causing testicular atrophy and male infertility. Younger men who may consider conceiving should be counseled regarding this possibility prior to taking these drugs.
- Sildenafil may cause headache and nausea.

CONTRAINDICATIONS

CONTRAINDICATIONS

In human immunodeficiency virus (HIV)-associated pulmonary arterial hypertension, oral anticoagulation is often contraindicated because of frequent hemostasis abnormalities and potential drug interactions between HIV medications and warfarin.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The information provided in the guideline should be used in conjunction with clinical judgment. Although the guideline provides recommendations that are based on evidence from studies involving various populations, the recommendations may not apply to every individual patient. It is important for the physician to take into consideration the role of patient preferences and the availability of local resources.
- The American College of Chest Physicians (ACCP) is sensitive to concerns that nationally and/or internationally developed guidelines are not always applicable in local settings. Further, guideline recommendations are just that, recommendations not dictates. In treating patients, individual circumstances, preferences, and resources do play a role in the course of treatment at every decision level. Although the science behind evidence-based medicine is rigorous, there are always exceptions. The recommendations are intended to guide healthcare decisions. These recommendations can be adapted to be applicable at various levels.

2007 Addendum

It should be noted that functional class is difficult to quantify, and may vary among patients and care providers. It may not always correlate with other indexes of disease severity, although it does correlate with outcome (in patients with idiopathic pulmonary arterial hypertension [IPAH]). Accordingly, decisions regarding therapy should take into account a variety of variables, including but not limited to functional class. Treating physicians should also consider cardiopulmonary hemodynamics, 6-minute walk (6MW) distance, signs and symptoms of right-heart failure, side effect profile, and drug-drug interactions when making recommendations to individual patients. Cost may be a consideration in the choice of therapy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation tools are being developed, including a quick reference guide in print and personal digital assistant format, and educational slide presentations for physicians and other health-care practitioners.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jul (addendum released 2007 Jun)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

Funding for both the evidence reviews and guideline development was provided through an unrestricted educational grant from GlaxoSmithKline, Texas Biotechnology Corporation, and Actelion Pharmaceuticals US. Representatives from these companies were not granted right of review, nor were they allowed participation in any portion of the guideline development.

GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on Pulmonary Artery Hypertension

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

2004 Guideline

Primary Authors: David B. Badesch, MD, FCCP, University of Colorado Health Sciences Center, Denver, CO; Steve H. Abman, MD, Children's Hospital, Denver, CO; Gregory S. Ahearn, MD, Duke University Medical Center, Durham, NC; Robyn J. Barst, MD, Columbia Presbyterian Medical Center, New York, NY; Douglas C. McCrory, MD, MHSc, Duke University Medical Center, Durham, NC; Gerald Simonneau, MD, Hospital Antoine Beclere, Clamart, France; Vallerie V. McLaughlin, MD, FCCP, Rush Presbyterian St. Lukes Hospital, Chicago, IL

2007 Addendum

Primary Authors: David B. Badesch, MD, FCCP; Steve H. Abman, MD; Gerald Simonneau, MD; Lewis J. Rubin, MD, FCCP; Vallerie V. McLaughlin, MD, FCCP

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The following participants have disclosed information regarding potential or real conflicts of interest and commitment:

2004 Guideline

Steven H. Abman, MD: scientific advisory board for INO Therapeutics; consultant for Pfizer.

Charles W. Atwood, Jr., MD, FCCP: research support from Respironics, Inc.

David B. Badesch, MD, FCCP: consultant or Speaker's Bureau for Glaxo Wellcome/GlaxoSmithKline, Actelion, InterMune, Encysive, Myogen, Astra-Merck, Astra-Zeneca, Exhale Therapeutics/CoTherix, Forrest Labs, INO Therapeutics, Berlex; research support from Glaxo Wellcome/GlaxoSmithKline, United Therapeutics, Boehringer Ingelheim, Actelion, Encysive, ICOS/Texas Biotechnologies/Encysive, Myogen, INO Therapeutics, Scleroderma Foundation, National Institutes of Health, National Heart, Lung, and Blood Institute, United Therapeutics, Pfizer, American Lung Association.

Robyn J. Barst, MD: consultant and research support from Actelion, Encysive, Exhale Therapeutics, INO, Myogen, United Therapeutics, Pfizer GlaxoSmithKline; unrestricted education grants from GlaxoSmithKline, Encysive, Actelion.

Richard N. Channick, MD, FCCP: research support from Actelion, Pfizer, Myogen, United Therapeutics; consultant and Speaker's Bureau for Actelion.

Ramona L. Doyle, MD, FCCP: Speaker's Bureau for Actelion; clinical research for Actelion, Myogen, United Therapeutics.

David D. Gutterman, MD, FCCP: stock options with Johnson & Johnson; relative who is a Vice-President at GlaxoSmithKline.

James E. Loyd, MD, FCCP: relationships with GlaxoSmithKline, United Therapeutics, Actelion, ICOS/Texas Biotechnology, Westat, PRA International, Pfizer, Exhale Therapeutics.

Michael D. McGoon, MD: past research support from Glaxo Wellcome, United Therapeutics, Actelion; research support from Texas Biotech/Encysive, Myogen, Pfizer, Medtronic.

Vallerie V. McLaughlin, MD, FCCP: consultant for Actelion, United Therapeutics, Exhale Therapeutics; Speaker's Bureau for Actelion; research funding from Actelion, United Therapeutics, Pfizer, Encysive/Texas Biotechnologies, Glaxo Wellcome, Exhale Therapeutics, Myogen.

Stuart Rich, MD: research funding from Actelion, Pfizer, United Therapeutics, Encysive, Myogen; consultant for Actelion, Pfizer, United Therapeutics, GlaxoSmithKline.

Lewis J. Rubin, MD, FCCP: consultant for Actelion, Myogen, Schering, Exhale Therapeutics, United Therapeutics, Pfizer, Celgene; investigator for Actelion, Myogen, Exhale, Pfizer, Celgene; no stock holdings or other ownerships or positions.

Gerald Simonneau, MD: consultant and investigator for Glaxo Wellcome, Pfizer, Actelion, Schering, Myogen, United Therapeutics.

Virginia D. Steen, MD: relationships with Arthritis Foundation, Scleroderma Foundation, Actelion.

Fredrick M. Wigley, MD: research funding from Biogen, Pfizer, Actelion; consultant to Genzyme.

2007 Addendum

Dr. Badesch has received grant monies from the National Institutes of Health. He has received grant monies from GlaxoSmithKline, United Therapeutics/LungRx, Actelion, Lilly/ICOS, Encysive, Pfizer, Myogen/Gilead, and CoTherix. He has received consultant fees from GlaxoSmithKline, Actelion, Myogen/Gilead, CoTherix, Pfizer, United Therapeutics, Mondo-Biotech, Biogen IDEC, PR Pharmaceuticals, Forrests Labs, Scios, Amgen, Biovale Pharmaceuticals/Clarus Health, and Johnson & Johnson. He has served on the speaker's bureau for GlaxoSmithKline, Actelion, Myogen/Gilead, Encysive, CoTherix, Pfizer, United Therapeutics, Mondo-Biotech, and Biogen IDEC. He has served on the board of directors for the Pulmonary Hypertension Association and the American Thoracic Society.

Dr. Abman has served as a scientific advisor for INO Therapeutics.

Dr. Simonneau has received grant monies from, served on the speaker's bureau for, and served on the advisory committees for Actelion, Pfizer, Schering, United Therapeutics, and GlaxoSmithKline.

Dr. Rubin has received university grant monies from the National Heart, Lung, and Blood Institute. He has received grant monies from Actelion, Pfizer, United Therapeutics, Mondo-Biotech, MD Primer, and Gilead. He is a shareholder in LungRx. He has received consultant fees from the National Heart, Lung, and Blood Institute; Actelion; Pfizer; United Therapeutics; ProQuest; Bayer Schering; and Mondo-Biotech. He is on the advisory committees for Actelion, Pfizer, LungRx, MD Primer, and Encysive.

Dr. McLaughlin has received grant monies from Actelion, Encysive, LungRx, Pfizer, and United Technologies. She has served on the speaker's bureau and advisory committees for Actelion, Gilead, and Pfizer.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies of the 2004 guideline and the 2007 addendum: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Background Articles

- Rubin, LJ. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Introduction. Chest 2004 Jul; 126(1 Suppl): 7S-10S.
- Rubin LJ. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. Executive summary. Chest 2004 Jul; 126(1 Suppl): 4S-6S.
- McCrory DC, Lewis SZ. Methodology and grading for pulmonary hypertension evidence review and guideline development. Chest 2004 Jul; 126(1 Suppl): 11S-13S.

Electronic copies: Available to subscribers of [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 27, 2004. This summary was updated by ECRI on July 15, 2005 following the FDA advisory on Cialis, Levitra, and Viagra. This summary was updated by ECRI on March 8, 2006 following the FDA advisory on Tracleer (bosentan). This summary was updated by ECRI on March 6, 2007 following the FDA advisory on Coumadin (warfarin sodium). This summary was updated by ECRI Institute on August 8, 2007 following the release of the addendum. This summary was updated by ECRI Institute on September 7, 2007 following the revised U.S. Food and Drug Administration (FDA) advisory on Coumadin (warfarin).

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